

## CLAIMS

1. Method of producing hollow microporous particles in particular intended to be inhaled or any other application characterised in that:
  - 5 - a composition is provided in a given form comprising at least one active principle and at least one expansion agent,
  - said composition is cooled at a temperature below the solidification point of said at least one expansion agent so as to increase the volume of the given form and to create fractures in the surface and/or in all of said given form,  
10 thereby enabling the structure of the hollow micro-porous particle to be obtained,
  - all or part of said at least one expansion agent is removed.
2. Method as claimed in Claim 1, wherein said composition in a given form is  
15 sprayed onto a cold medium having a temperature lower than said solidification point of said at least one expansion agent.
3. Method as claimed in Claim 1, wherein said at least one expansion agent has  
20 an expansion coefficient greater than 5%.
4. Method as claimed in Claims 1 to 3, wherein said at least one expansion agent is selected from the group consisting of methanol, dichloromethane, acetone, and mixtures thereof.
- 25 5. Method as claimed in Claims 1 to 3, wherein said at least one expansion agent is selected from the group of gas consisting of carbon dioxide, nitrogen, carbonate, bicarbonate, carboxylic acid and derivatives thereof.
6. Method as claimed in any one of the preceding Claims, wherein said active  
30 principle is selected from the group consisting of proteins, lipids, nucleic acid, short chain peptide, corticosteroids, anti-inflammatories, analgesics, anti-neoplastic agents or bronchodilators.
7. Method as claimed in any one of the preceding Claims, wherein said active

principle is a steroid selected from the group consisting of budesonide, testosterone, progesterone, oestrogen, flunisolide, triamcinolone, beclomethasone, betamethasone, dexamethasone, fluticasone, methyl-prednisolone, prednisone and hydrocortisone.

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8. Method as claimed in one of Claim 7, wherein the active principle is beclomethasone dipropionate (BDP).
9. Method as claimed in Claim 6, wherein said active principle is a  
10 bronchodilator selected from the compounds ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, perbuterol, reproterol, rimeterol, salbutamol, salmeterol, formoterol, terbutaline, isoetharine, tulobuterol, orciprenaline or  
15 (-)-4-amino-3,5-dichloro- $\alpha$ [[[6-[2-(pyridinyl)ethoxy}hexyl]amino]methyl]benzenemethanol.
10. Method as claimed in Claim 9, wherein said active principle is salbutamol sulphate.
- 20 11. Method as claimed in Claim 2, wherein the spraying step is carried out by atomising said composition in the form of droplets.
12. Method as claimed in the preceding Claim, wherein atomisation is carried out using pneumatic means, ultrasonic means, pressurized means, nozzle means,  
25 rotary atomiser means, blowing means, high rotational generators, spraying devices, gauge needles or a hair-dryer.
13. Method as claimed in the preceding Claim, wherein the atomisation gas is selected from the group consisting of carbon dioxide, nitrogen, argon, oxygen,  
30 air and mixtures thereof.
14. Method as claimed in any one of the preceding Claims, wherein the cooling step is carried out by means of a gas selected from the group consisting of

liquid hydrogen, liquid nitrogen, liquid oxygen.

15. Method as claimed in any one of the preceding Claims, wherein furthermore said particles are dried using blowing means, oven, vacuum oven, fluid bed dryer.
16. Method as claimed in Claim 15, wherein the drying step comprises the evaporation of said at least one expansion agent.
17. Method as claimed in Claim 15, wherein the drying step comprises the lyophilisation of the particles.
18. Method as claimed in any one of the preceding Claims, wherein the composition comprises a mixture of acetone and water in a ratio of 80 : 20 volume/volume.
19. Method as claimed in any one of the preceding Claims, wherein the composition further comprises at least one additional excipient.
20. Method as claimed in Claim 19, wherein said at least one additional excipient is a polymer compound permitting the density to be altered and the action of said at least one active principle to be slowed, controlled or targeted.
21. Method as claimed in Claim 19, wherein said at least one additional excipient is selected from the following compounds: cyclodextrins and derivatives thereof, sodium caseinate, DPPC, serum albumin, cellulose acetate phthalate, phospholipids, hydroxypropyl methylcellulose phthalate, ethyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, carboxymethyl cellulose, methyl cellulose, cellulose acetate butyrate, poloxamer, poly(lactic acid), poly(lactic glycolic acid), poly(lactide), poly(glycolide), poly(lactide-coglycolide), poly(p-dioxanone), poly(caprolactone), polycarbon, polyamide, polyanhydride, poly(alkylene alkylate), polyamino acid, polyhydroxyalkanoates, polypropylenefumarates, polyorthoester, polyacetal, polyacrylamide,

polycyanoacrylate, polyalkylcyanoacrylates, polymethapolyphosphate ester, polyphosphazene, polyurethane, polyacrylate, polymethacrylate, poly(methyl methacrylate), poly(hydroxy ethyl methacrylate - co methyl methacrylate, carbopol 934, ethylene-vinyl acetate and other substituted acyl cellulose acetates and derivatives thereof, polystyrene, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonated polyolefin, polyethylene, polyethylene glycol, polypropylene, polyethylene oxide, copolymer and blends thereof, cellulose acetate phthalate (CAP) and hydroxypropyl cellulose acetate phthalate.

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22. Hollow microporous particles produced by the method as claimed in any one of Claims 1 to 21, having particles measuring between 0.1  $\mu\text{m}$  and 2000  $\mu\text{m}$  and whose density is in the range from 0.4  $\text{g/cm}^3$  to 0.0001  $\text{g/cm}^3$ .

15 23. Medicine, intended to be administered by inhalation, having the microporous particles as claimed in Claim 22.

24. Use of said hollow microporous particles as claimed in Claim 22 in the production of a medicine for treating respiratory diseases.

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25. Inhalation device having the hollow microporous particles obtained by the method as claimed in any one of Claims 1 to 21.